CLAIMS

1. An isolated MAGE-A1 HLA class II-binding peptide comprising a fragment of the amino acid sequence of SEQ ID NO:2 which binds an HLA class II molecule, or a functional variant thereof comprising one or more amino acid additions, substitutions or deletions.

2. The isolated HLA class II-binding peptide of claim 1 wherein the isolated peptide comprises the amino acid sequence set forth as SEQ ID NO:7 or a functional variant thereof.

3. The isolated HLA class II-binding peptide of claim 2 wherein the isolated peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4, and SEQ ID NO:7.

4. The isolated HLA class II-binding peptide of claim 2 wherein the isolated peptide consists of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

5. The isolated HLA class II-binding peptide of claim 1 wherein the isolated peptide comprises an endosomal targeting signal.

6. The isolated HLA class II-binding peptide of claim 5 wherein the endosomal targeting signal comprises an endosomal targeting portion of human invariant chain Ii or LAMP-1.

7. The isolated HLA class II-binding peptide of claim 1 wherein the isolated peptide is non-hydrolyzable.

8. The isolated HLA class II-binding peptide of claim 7 wherein the isolated peptide is selected from the group consisting of peptides comprising D-amino acids, peptides comprising a -psi[CH_2NH]-reduced amide peptide bond, peptides comprising a -psi[$COCH_2$]-ketomethylene peptide bond, peptides comprising a -psi[CH(CN)NH]-(cyanomethylene)amino peptide bond, peptides comprising a -psi[$CH_2CH(OH)$]-hydroxyethylene peptide bond, peptides comprising a -psi[CH_2O]-peptide bond, and peptides comprising a -psi[CH_2S]-thiomethylene peptide bond.

9. A composition comprising an isolated MAGE-A1 HLA class I-binding peptide and an isolated MAGE-A1 HLA class II-binding peptide.

10. The composition of claim 9 wherein the MAGE-A1 HLA class I-binding peptide and the MAGE-A1 HLA class II-binding peptide are combined as a polytope polypeptide.

~~11. The composition of claim 9 wherein the isolated MAGE-A1 HLA class II-binding peptide comprises the amino acid sequence of SEQ ID NO:7 or a functional variant thereof.~~

12. The composition of claim 11 wherein the isolated MAGE-A1 HLA class II-binding peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

13. The composition of claim 11 wherein the isolated MAGE-A1 HLA class II-binding peptide consists of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

14. The composition of claim 9 wherein the isolated MAGE-A1 HLA class II-binding peptide comprises an endosomal targeting signal.

15. The composition of claim 14 wherein the endosomal targeting signal comprises an endosomal targeting portion of human invariant chain Ii or LAMP-1.

16. An isolated nucleic acid encoding a peptide selected from the group consisting of the peptide of claim 1, the peptide of claim 2, the peptide of claim 3, the peptide of claim 4, and the peptide of claim 5.

17. The isolated nucleic acid of claim 16 wherein the nucleic acid comprises a nucleotide sequence set forth as SEQ ID NO:12.

18. An expression vector comprising the isolated nucleic acid of claim 17 operably linked to a promoter.

19. The expression vector of claim 18 wherein the nucleic acid consists of a nucleotide sequence set forth as SEQ ID NO:12.

20. The expression vector of claim 18 further comprising a nucleic acid which encodes an HLA-DRB1*15 molecule.

21. A host cell transfected or transformed with an expression vector selected from the group consisting of the expression vector of claim 18, the expression vector of claim 19, and the expression vector of claim 20.

22. A host cell transfected or transformed with an expression vector selected from the group of the expression vector of claim 18 and the expression vector of claim 19, and wherein the host cell expresses an HLA-DRB1*15 molecule.

23. A method for enriching selectively a population of T lymphocytes with $CD4^+$ T lymphocytes specific for a MAGE-A1 HLA class II-binding peptide comprising:

contacting an isolated population of T lymphocytes with an agent presenting a complex of the MAGE-A1 HLA class II-binding peptide and an HLA class II molecule in an amount sufficient to selectively enrich the isolated population of T lymphocytes with the $CD4^+$ T lymphocytes.

24. The method of claim 23, wherein the agent is an antigen presenting cell contacted with a MAGE-A1 protein or an HLA class II binding fragment thereof.

25. The method of claim 23 or 24 wherein the HLA class II molecule is an HLA-DRB1*15 molecule and wherein the MAGE-A1 HLA class II-binding peptide comprises an amino acid sequence set forth as SEQ ID NO:7 or a functional variant thereof.

26. The method of claim 23 or 24 wherein the HLA class II molecule is an HLA-DRB1*15 molecule and wherein the MAGE-A1 HLA class II-binding peptide comprises of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4, and SEQ ID NO:7.

27. The method of claim 23 or 24 wherein the HLA class II molecule is an HLA-DRB1*15 molecule and wherein the MAGE-A1 HLA class II-binding peptide consists of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

28. The method of claim 24 wherein the MAGE-A1 protein or HLA class II binding peptide thereof comprises an endosomal targeting portion of human invariant chain Ii or LAMP-1.

29. A method for diagnosing a disorder characterized by expression of MAGE-A1 comprising:

contacting a biological sample isolated from a subject with an agent that is specific for the MAGE-A1 HLA class II binding peptide, and

determining the interaction between the agent and the MAGE-A1 HLA class II binding peptide as a determination of the disorder.

30. The method of claim 29 wherein the MAGE-A1 HLA class II-binding peptide comprises an amino acid sequence set forth as SEQ ID NO:7 or a functional variant thereof.

31. The method of claim 30 wherein the MAGE-A1 HLA class II-binding peptide comprises of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

32. The method of claim 30 wherein the MAGE-A1 HLA class II-binding peptide consists of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

33. A method for diagnosing a disorder characterized by expression of a MAGE-A1 HLA class II-binding peptide which forms a complex with an HLA class II molecule, comprising:

contacting a biological sample isolated from a subject with an agent that binds the complex; and

determining binding between the complex and the agent as a determination of the disorder.

34. The method of claim 33 wherein the HLA class II molecule is an HLA-DRB1/13 molecule and the MAGE-A1 HLA class II-binding peptide comprises an amino acid set forth as SEQ ID NO:7 or a functional variant thereof.

35. The method of claim 34 wherein the MAGE-A1 HLA class II-binding peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

36. The method of claim 34 wherein the MAGE-A1 HLA class II-binding peptide consists of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

37. A method for treating a subject having a disorder characterized by expression of MAGE-A1, comprising:

administering to the subject an amount of a MAGE-A1 HLA class II-binding peptide sufficient to ameliorate the disorder.

38. The method of claim 37 wherein the MAGE-A1 HLA class II binding peptide comprises an endosomal targeting signal.

39. The method of claim 38 wherein the endosomal targeting signal comprises an endosomal targeting portion of human invariant chain Ii or LAMP-1.

40. The method of claim 38 wherein the MAGE-A1 HLA class II-binding peptide comprises an amino acid sequence set forth as SEQ ID NO:7 or a functional variant thereof.

41. The method of claim 40 wherein the MAGE-A1 HLA class II-binding peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4, and SEQ ID NO:7.

42. The method of claim 40 wherein the MAGE-A1 HLA class II-binding peptide consists of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

43. A method for treating a subject having a disorder characterized by expression of MAGE-A1, comprising:

administering to the subject an amount of a MAGE-A1 HLA class I-binding peptide and an amount of a MAGE-A1 HLA class II-binding peptide sufficient to ameliorate the disorder.

44. The method of claim 43 wherein the MAGE-A1 HLA class I-binding peptide and the MAGE-A1 HLA class II-binding peptide are combined as a polytope polypeptide.

45. The method of claim 43 wherein the MAGE-A1 HLA class II binding peptide comprises an endosomal targeting signal.

46. The method of claim 45 wherein the endosomal targeting signal comprises an endosomal targeting portion of human invariant chain Ii.

47. The method of claim 43 wherein the MAGE-A1 HLA class II-binding peptide comprises an amino acid sequence set forth as SEQ ID NO:7 or a functional variant thereof.

48. The method of claim 47 wherein the MAGE-A1 HLA class II-binding peptide comprises of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

49. The method of claim 47 wherein MAGE-A1 HLA class II-binding peptide consists of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

50. A method for treating a subject having a disorder characterized by expression of MAGE-A1, comprising:

administering to the subject an amount of an agent which enriches selectively in the subject the presence of complexes of an HLA class II molecule and a MAGE-A1 HLA class II-binding peptide, sufficient to ameliorate the disorder.

51. The method of claim 50 wherein the HLA class II molecule is an HLA-DRB1*15 molecule and the MAGE-A1 HLA class II-binding peptide comprises an amino acid set forth as SEQ ID NO:7 or a functional variant thereof.

52. The method of claim 51 wherein the MAGE-A1 HLA class II-binding peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

53. The method of claim 51 wherein the MAGE-A1 HLA class II-binding peptide consists of an amino acid sequence selected from the group ~~consisting~~ of SEQ ID NO:3, SEQ ID NO:4, and SEQ ID NO:7.

54. The method of claim 50 wherein the agent comprises a MAGE-A1 HLA class II binding peptide.

55. The method of claim 54 wherein the MAGE-A1 HLA class II binding peptide comprises an endosomal targeting signal.

56. The method of claim 55 wherein the endosomal targeting signal comprises an endosomal targeting portion of human invariant chain Ii or LAMP-1.

57. A method for treating a subject having a disorder characterized by expression of MAGE-A1, comprising:

administering to the subject an amount of autologous $CD4^+$ T lymphocytes sufficient to ameliorate the disorder, wherein the $CD4^+$ T lymphocytes are specific for complexes of an HLA class II molecule and a MAGE-A1 HLA class II-binding peptide.

58. The method of claim 57 wherein the HLA class II molecule is an HLA-DRB1/13 molecule and the MAGE-A1 HLA class II-binding peptide comprises an amino acid sequence set forth as of SEQ ID NO:7 or a functional variant thereof.

59. The method of claim 58 wherein the MAGE-A1 HLA class II-binding peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

60. The method of claim 58 wherein the MAGE-A1 HLA class II-binding peptide consists of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

61. A method for identifying functional variants of a MAGE-A1 HLA class II binding peptide, comprising

selecting a MAGE-A1 HLA class II binding peptide, an HLA class II binding molecule which binds the MAGE-A1 HLA class II binding peptide, and a T cell which is stimulated by the MAGE-A1 HLA class II binding peptide presented by the HLA class II binding molecule;

mutating a first amino acid residue of the MAGE-A1 HLA class II binding peptide to prepare a variant peptide;

determining the binding of the variant peptide to HLA class II binding molecule and the stimulation of the T cell, wherein binding of the variant peptide to the HLA class II binding molecule and stimulation of the T cell by the variant peptide presented by the HLA class II binding molecule indicates that the variant peptide is a functional variant.

62. The method of claim 61 wherein the MAGE-A1 HLA class II-binding peptide comprises an amino acid sequence set forth as SEQ ID NO:7.

63. The method of claim 61 further comprising the step of comparing the stimulation of the T cell by the MAGE-A1 HLA class II binding peptide and the stimulation of the T cell by the functional variant as a determination of the effectiveness of the stimulation of the T cell by the functional variant.

64. An isolated polypeptide which binds selectively a polypeptide having an epitope comprising SEQ ID NO:7, provided that the isolated polypeptide is not an HLA class II molecule.

65. The isolated polypeptide of claim 64 wherein the isolated polypeptide is an antibody.

66. The antibody of claim 65 wherein the antibody is a monoclonal antibody.

67. The isolated polypeptide of claim 64 wherein the isolated polypeptide is an antibody fragment selected from the group consisting of a Fab fragment, a $F(ab)_2$ fragment or a fragment including a CDR3 region selective for a MAGE-A1 HLA class II-binding peptide.

68. An isolated $CD4^+$ T lymphocyte which selectively binds a complex of an HLA class II molecule and a MAGE-A1 HLA class II-binding peptide.

69. The isolated $CD4^+$ T lymphocyte of claim 68 wherein the HLA class II molecule is an HLA-DRB1*15 molecule and wherein the MAGE-A1 HLA class II-binding peptide comprises an amino acid sequence set forth as SEQ ID NO:7 or a functional variant thereof.

70. The isolated $CD4^+$ T lymphocyte of claim 69 wherein the MAGE-A1 HLA class II-binding peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

71. The isolated $CD4^+$ T lymphocyte of claim 69 wherein the MAGE-A1 HLA class II-binding peptide consists of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

72. An isolated antigen presenting cell which comprises a complex of an HLA class II molecule and a MAGE-A1 HLA class II-binding peptide.

73. The isolated antigen presenting cell of claim 72 wherein the HLA class II molecule is an HLA-DRB1*15 molecule and wherein the MAGE-A1 HLA class II-binding peptide comprises an amino acid sequence set forth as SEQ ID NO:7 or a functional variant thereof.

74. The isolated antigen presenting cell of claim 73 wherein the MAGE-A1 HLA class II-binding peptide comprises of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.

75. The isolated antigen presenting cell of claim 73 wherein the MAGE-A1 HLA class II-binding peptide consists of an amino acid sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:7.